

Direct-to-Consumer Provider Primer: Incidental and Secondary Findings

In December 2013, the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) released its report, [*Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*](#). The report outlines the types of findings that can arise from various tests and procedures in a variety of contexts, and makes 17 recommendations for the ethical and professional management of such findings.

This primer was designed to help direct-to-consumer (DTC) providers understand and implement the Bioethics Commission's recommendations regarding how to manage incidental and secondary findings ethically in the DTC setting. DTC providers can use it to aid ethical decision making and to address common questions about incidental and secondary findings and their ethical management. In addition, the final page of this primer provides a list of considerations to help DTC companies evaluate whether they have prepared fully for the management of incidental and secondary findings. Please see *Anticipate and Communicate* for further reading on the Bioethics Commission's analysis and recommendations (Executive Summary, pp. 2-20 and Chapter 6, pp. 95-110). This primer and the list of considerations are not derived from regulations. Rather, the primer reflects the Bioethics Commission's recommendations regarding the ethical management of incidental and secondary findings.

DTC providers should have clearly written materials that are easily accessible by consumers, including contracts, terms of service, and Internet-based portals that address which findings will be sought and which findings, if any, will be returned to consumers. DTC providers should also consider developing best practices regarding disclosure of incidental findings and when secondary findings should be sought deliberately, including the types of findings that ought to be disclosed and the methods for communicating these findings. DTC providers can find further guidance regarding these elements below.

FREQUENTLY ASKED QUESTIONS

1. What are incidental and secondary findings?

Incidental findings traditionally are defined as results that are outside the original purpose for which a test or procedure was conducted. These are distinct from *primary findings*, which are the results that are actively sought as the primary target of a test or procedure.

Incidental findings can be either “anticipatable” or “unanticipatable.” An *anticipatable incidental finding* is one that is known to be associated with a test or procedure. Anticipatable incidental

findings need not be common or even likely to occur—their defining characteristic is that the possibility of finding them is known.

Unanticipatable incidental findings include findings that could not have been anticipated given the current state of scientific knowledge. Providers cannot plan for these types of findings specifically. However, they can consider in advance what they might do if a particular kind of unexpected finding arises, for example, one that could be actionable or lifesaving.

A *secondary finding*, by contrast, is not the primary target of the test or procedure; rather, it is an additional result actively sought by the practitioner. Secondary findings might be sought deliberately when doing so is recommended by an expert body or by a consensus of practitioners.

Discovery findings are the results of a broad test that aims to discover everything of interest. These kinds of findings are particularly common in the DTC industry. For example, “wellness scans” that offer whole body CT or MRI imaging are marketed to consumers who aim to discover everything of interest, including abnormalities, signs of cancer, and any indication of disease. Although *Anticipate and Communicate* did not explicitly grapple with the ethical issues surrounding discovery findings, it is important to note that discovery findings can be sensitive or surprising to the consumer, and thus should be handled with care. The following table provides examples of each type of finding.

Bioethics Commission Classification of Individualized Results of Medical Tests

TYPE OF RESULT DISCOVERED	DESCRIPTION	EXAMPLE
Primary Finding	Practitioner aims to discover A, and result is relevant to A	In a child with unknown vaccine history, a test done to determine a child's immunity status before the chickenpox vaccine is administered
Incidental Finding: Anticipatable	Practitioner aims to discover A, but learns B, a result known to be associated with the test or procedure at the time it takes place	Discovering misattributed paternity when assessing a living kidney donor and potential recipient who believe they are biologically related
Incidental Finding: Unanticipated	Practitioner aims to discover A, but learns C, a result not known to be associated with the test or procedure at the time it takes place	When a DTC genetic testing company identifies a health risk based on a newly discovered genetic association not knowable at the time a previous sample was submitted
Secondary Finding	Practitioner aims to discover A, and also actively seeks D per expert recommendation	ACMG recommends that laboratories conducting large-scale genetic sequencing for any purpose should actively look for variants underlying 24 phenotypic traits
Discovery Finding	Practitioner aims to discover A through Z by employing a test or procedure designed to detect a broad array of results	A "wellness scan," a whole body computed tomography (CT) scan, is intended to discover any abnormal finding throughout the body

Source: Presidential Commission for the Study of Bioethical Issues (PCSB). (2013, December). *Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts*. Washington, DC: PCSBI, p. 27. Note: DTC = direct-to-consumer, ACMG = American College of Medical Genetics and Genomics.

2. What are some of the tests or procedures that could give rise to incidental and secondary findings?

A variety of tests and procedures can give rise to incidental and secondary findings. Examples include:

- Large-Scale Genetic Sequencing:** Genetic sequencing is the analysis and ordering of the billions of base pairs—the As, Ts, Cs, and Gs—that make up the human genome. Large-scale genetic sequencing techniques include whole genome sequencing, whole exome sequencing, and other next-generation genomic analyses. Because of the large number of base pairs sequenced and potentially analyzed, large-scale genetic sequencing has the potential to yield large numbers of incidental and secondary findings. While some variants discovered during large-scale genetic sequencing reveal clinically relevant information, much of the data produced are of unknown or uncertain medical value. In addition, incidental and secondary findings that arise in genetic sequencing also can have implications for biologically-linked family members.

- **Testing of Biological Specimens:** Analysis of biological specimens such as blood, urine, or bodily tissues can be a source of incidental or secondary findings. Incidental and secondary findings arising from blood and tissue testing could definitively indicate a health issue of concern, or could require a series of additional diagnostic tests to determine the health implications, if any, of the result. For example, a researcher might order a metabolic panel to assess kidney function, but the laboratory results might reveal an incidental finding of liver dysfunction.
- **Imaging:** Medical imaging includes magnetic resonance imaging (MRI), computed tomography (CT) scans, X-rays, neuroimaging, and ultrasounds, among others. The images produced provide visualization of an entire field of study and can give rise to incidental and secondary findings in areas outside the area of diagnostic interest. For example, scans of the abdomen and pelvis can include images of the kidneys, liver, adrenal glands, and pancreas, only one of which might be the organ of interest.

3. What are the responsibilities to consumers of a DTC provider that offers tests and procedures likely to give rise to incidental and secondary findings?

Potential recipients of incidental and secondary findings should be informed about the likelihood of these findings arising from a particular test or procedure. Providing this information in advance of the test or procedure enables a potential recipient to decide whether and how to proceed. It facilitates trust and can help decrease anxiety and confusion about results.

To enable consumers to make responsible and informed choices regarding DTC testing, consumers must be told what these procedures entail, including the possibility of incidental and secondary findings. Information provided before selecting a DTC procedure can assist consumers in deciding what services are worth pursuing.

DTC providers must inform consumers considering their services about the procedures and results included in the commercial arrangement. Among the information needed by consumers is an understanding of the anticipatable incidental findings commonly associated with particular modalities and any secondary findings that will be sought. If certain results are not returned according to company policy or contractual agreement, this must be disclosed to consumers as well.

The following table of ethical principles and their application to incidental and secondary findings can help DTC providers determine their ethical responsibilities.

Ethical Principles in the DTC Context

<i>Principle</i>	<i>Definition</i>	<i>Application</i>
Respect for Persons	This principle recognizes the fundamental human capacity for rational self-determination.	DTC testing enables consumers to exercise greater control over what they know about themselves. The materials provided should include whether and how DTC companies intend to disclose and manage incidental and secondary findings.
Beneficence	This principle calls on professionals to take action to ensure the wellbeing of others. Its corollary, non-maleficence, requires not imposing harm on others.	In the DTC context, disclosure of clinically actionable and significant incidental and secondary findings might fall within the basic duty to warn. Given that DTC providers have a relationship with consumers, and that those with clinical expertise who provide DTC testing retain some fiduciary duties even for tests conducted outside of the clinic, the duties of DTC providers could extend even beyond this minimal duty to warn.
Justice and Fairness	This principle requires fair and equitable distribution of benefits and burdens across society.	The principle of justice and fairness requires consideration of whether it is reasonable for consumers to expect that DTC providers will return incidental and secondary findings even if not explicitly delineated in a contract.
Intellectual Freedom and Responsibility	This principle protects sustained and dedicated creative intellectual exploration that furthers scientific progress, while requiring that practitioners take responsibility for their actions.	The exercise of intellectual freedom is expressed through the innovation and ingenuity necessary to make advances in the development and provision of DTC testing services. DTC providers also have a corresponding responsibility to conscientiously manage incidental and secondary findings.

4. What are the responsibilities of a DTC provider that offers tests and procedures likely to give rise to incidental and secondary findings to the DTC professional community?

DTC providers are uniquely positioned to understand the nature of their own industry. This knowledge enables DTC providers to develop best practices that are consistent with relevant ethical principles. For example, DTC providers who discover clinically actionable incidental or secondary findings with health implications could provide consumers with educational information about the nature of the finding, advice about how best to seek care from a clinician or specialist, or even a referral to a clinician who could assist in the management of the finding.

If providers adopt voluntary best practices, such best practices could become standard expectations for consumers who choose to undergo DTC testing, giving other companies incentive to adopt and implement these practices, thereby providing ethical services to consumers whichever company they choose to patronize.

DTC providers should develop best practices regarding disclosure of incidental findings and when secondary findings should be sought, including the types of findings that ought to be disclosed and the methods for communicating these findings. Companies should make these “best practices” publicly available to encourage broader adoption.

For particularly sensitive findings, DTC providers could adopt certain procedural safeguards, especially if they do not provide counseling similar to that which might be standard practice in a clinical setting. As an example, a DTC provider might require that consumers pass through several layers of information on its web portal to access highly sensitive results. This kind of procedural safeguard might help consumers manage their anxiety and confusion about receiving certain results.

Considerations for Ethical Management of Incidental and Secondary Findings

- Consider the various incidental and secondary findings that can arise from the test or procedure that is being conducted.
- Develop a plan for managing these incidental and secondary findings. Answers to the following questions will help inform such a plan:
 - Will findings be actively sought?
 - Will findings be communicated to consumers? If so, how?
 - What, if any, follow-up is needed?
 - Who will be responsible for that follow-up?
- Make information about the plan for managing incidental and secondary findings easily available to the consumer (e.g., in accessible and comprehensive terms of service or in company contracts or other documents).